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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,656	06/20/2003	Bill E. Cham	13131-0310 (44378-282108)	8075
23370 7590 08/17/2007 JOHN S. PRATT, ESQ KILPATRICK STOCKTON, LLP 1100 PEACHTREE STREET ATLANTA, GA 30309				
EXAMINER CHEN, STACY BROWN				
ART UNIT		PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/601,656

Applicant(s)

CHAM ET AL.

Examiner

Stacy B. Chen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,28-31 and 33-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,28-31 and 33-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 June 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/311,679.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 20, 2007 has been entered. Claims 1, 2, 28-31 and 33-54 are pending and under examination.

Priority

2. The Office notes that the instant claims have priority to provisional application, USSN 60/390,066, filed June 20, 2002. The instant claims are drawn to subject matter that was not present in the parent application, USSN 10/311,679. The subject matter that is entitled only to the benefit of the filing date of the provisional application is, "at least one exposed epitope not usually presented to an immune system of the animal or the human by the non-delipidated viral particle".

Applicant's remarks regarding the priority of the claimed invention have been considered. Applicant specifically notes that 10/311,679 discloses immunodeficiency viruses and vaccines. In response, the disclosure of immunodeficiency viruses and vaccines is not sufficient to adequately describe "at least one exposed epitope not usually presented to an immune system of the animal or the human by the non-delipidated viral particle", as recited in

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the claims. Therefore, the art rejections are based on the date of priority for this application, June 20, 2002.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48 and 52 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Prior to the amendment of June 20, 2007, the claims recited a range of concentration (“0.3% to 2.5%”) that did not appear to have been contemplated in the specification or the claims as originally filed. In the amendment of June 20, 2007, Applicant amended the claims to recite a range of concentration, “0.5% to 2.5%”, was previously presented in the amendment filed March 3, 2006. In the subsequent Office action of April 17, 2006, the Office did not reject the claims reciting that range on the basis of new matter. However, upon further consideration of the specification, the claims are rejected for reciting a range that does not appear to have been contemplated in the specification or claims as originally filed.

Claim 48 encompasses a range of concentration of an organic solvent generally, of 0.5% to 2.5%. The specification does not contemplate this range in the context of solvents generally,

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only specifically with regard to ethers. Paragraph [0104] of the PGPub of this application, US 2004/0170649A1 is reproduced below:

[0104] Low concentrations of ethers may be employed to remove lipids when used alone and not in combination with other solvents. For example, a low concentration range of ethers include 0.5% to 30%. Such concentrations of ethers that may be employed include, but are not limited to the following: 0.625%, 1.0%, 1.25%, 2.5%, 5.0% and 10% or higher. It has been observed that dilute solutions of ethers are effective. Such solutions may be aqueous solutions or solutions in aqueous buffers, such as phosphate buffered saline (PBS). Other physiological buffers may be used, including but not limited to bicarbonate, citrate, Tris, Tris/EDTA, and Trizma. Preferred ethers are di-isopropyl ether (DIPE) and diethyl ether (DEE).

When speaking of solvents generally, the specification contemplates a range of 0.5% to 4.0%, for example. Paragraph [0114] of the PGPub of this application, US 2004/0170649A1 is reproduced below:

[0114] Once a biological fluid, such as plasma, is obtained either in this manner, or for example, from a storage facility housing bags of plasma, the plasma is contacted with a first organic solvent, as described above, capable of solubilizing lipid in the lipid-containing infectious organism. The first organic solvent is combined with the plasma in a ratio wherein the first solvent is present in an amount effective to substantially solubilize the lipid in the infectious organism, for example, dissolve the lipid envelope that surrounds the virus. Exemplary ratios of first solvent to plasma (expressed as a ratio of first organic solvent to plasma) are described in the following ranges: 0.5-4.0:0.5-4.0; 0.8-3.0:0.8-3.0; and 1-2:0.8-1.5. Various other ratios may be applied, depending on the nature of the biological fluid. For example, in the case of cell culture fluid, the following ranges may be employed of first organic solvent to cell culture fluid: 0.5-4.0:0.5-4.0; 0.8-3.0:0.8-3.0; and 1-2:0.8-1.5.

Therefore, the rejection is maintained because the specification does not appear to have contemplated a general range of 0.5% to 2.5% with regard to solvents generally, only with specific regard to ethers.

Claims Summary

4. The claims are drawn to a modified virus particle, specifically from an immunodeficiency virus pathogen, comprising at least a partially delipidated immunodeficiency virus particle that initiates a positive immune response in an animal or human patient and incites protection against an infectious organism. The specification indicates that the viral particle is modified by exposing a non-delipidated viral particle to a delipidation process wherein the lipid content of a virus is reduced. The particle is partially delipidated by treating a lipid-containing virus particle with an organic solvent that is not a detergent or a surfactant. The particle is not infectious, yet remains immunogenic and exposes epitopes that are not usually presented to the immune system by untreated virus. The virus particle proteins are structurally changed by the delipidation process on, in or near the surface of the virus (page 20, lines 10-23). Particular epitopes include gag, p6, gp66, gp41, p27 or env. The modified viral particle retains over 90% of major protein constituents.

Claim Rejections - 35 USC § 102/103

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 28-31 and 33-54 are rejected under 35 U.S.C. 102(b) as being anticipated by, or rendered obvious under 35 U.S.C. 103(a) by Barrett et al. (US 6,136,321, "Barrett", filed February 10, 1998). Barrett discloses a method of inactivating lipid-enveloped viruses. The

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method involves a non-ionic detergent from the group of polysorbates for a period of time to completely inactivate the virus particle without affecting its structural integrity and particularly the biological activity of its surface and envelope proteins (col. 3, lines 1-15). Viruses that are inactivated by the disclosed method include all enveloped viruses, including retroviruses, such as SIV, HIV-1 and HIV-2 (col. 2, lines 50-59, and col. 3, lines 38-45). Barrett discloses that the biological activity of HIV's CD4 binding function is not affected by the inactivation (col. 3, lines 50-52).

In Examples 1-3, Barrett describes the inactivation of HIV-1, HIV-2, influenza and pseudorabies virus (PRV). The viruses are purified via sucrose gradient centrifugation and dialysis. The purified preparation is admixed with octyl glucoside or polysorbate 80 for one hour. The presence of HIV proteins was measured after the inactivation, and gp120 and gp140 were detected.

Barrett uses polysorbate 80 in particular because it is considered to be compatible for humans and is frequently used in foods and cosmetics (col. 5, lines 12-18). The concentration of the polysorbate is in a range of between 1% and 25%. Barrett also discloses that the inactivated virus may be formulated with pharmaceutically acceptable and physiologically acceptable carriers, such as ionized water, PBS, salts, amino acids and non-ionic detergents for stabilizing purposes (col. 6, lines 14-27). The composition may also contain an adjuvant (immunostimulant) such as mineral oils, immunomodulators and immunopotentiators (col. 6, lines 28-37).

Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does

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not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.

The claimed method steps of making the compositions do not lend patentability to the claims. The method steps are not expected to result in a structurally different and functionally different product than Barrett because the method steps of Barrett use the same organic solvent that Applicant has indicated as useful in the production of partially delipidated viral particles: polysorbates (surfactants). *Even though the claims have been amended such that detergents and surfactants are not used to delipidate the virus particles, the effect of the detergents and the surfactants is expected to be the same as the other solvents encompassed by the claims.* The detergents, surfactants and the other solvents are functional equivalents, since they were/are included in a Markush group. Even in the claims that recite alcohols as the organic solvent, one expects the resulting viral particle to be the same as Barrett's viral particle that has reduced lipid content yet remains biologically active. Therefore, the invention as a whole is anticipated by the prior art.

Response to Arguments

6. Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Barrett uses non-ionic surfactants, particularly polysorbate, for inactivated lipid enveloped viruses. Applicant asserts that Barrett does not disclose partially delipidated virus particles and is silent as to the lipid content in its viral particles.

Applicant argues that the examiner's assertion that one would expect that viral particles disclosed in Barrett (treated with a detergent) to be the same as the viral particles partially delipidated with an alcohol, is not supported with evidence. Applicant argues that Barrett does not teach or suggest any characteristics of Applicant's claimed particles recited in the claims.

- In response to Applicant's arguments, the instant claims are drawn to products. The products of Barrett and the products instantly claimed are viral particles whose envelope lipid content has been altered such that the viral particles have been modified. Although Barrett does not discuss the actual lipid content of the viruses treated with polysorbate, the resulting viral particle structure is expected to be the same as Applicant's particle because Applicant discloses that detergents/surfactants may be used (page 27, lines 12-13) to delipidate viruses.
- Applicant points out that Barrett teaches in col. 2, lines 46-49, that the detergent replaces the lipids that are normally connected to the hydrophobic portion of the proteins. In col. 5, lines 38-40, Barrett discloses the use of a stabilizing agent, the only example of which is polysorbate at a final concentration of at least 0.05% (Barrett, col. 5, lines 31-47, and col. 6, lines 1-8). *Applicant argues that although Barrett suggests removing a detergent from a viral solution after delipidation by a detergent, there is no teaching or suggestion to remove the detergent molecules that replaced the lipids* (col. 5, lines 11-30). Applicant points out that Barrett's particles necessarily contain detergent in place of lipid in their viral envelopes. This is in contrast to Applicant's particles, where lipids are simply partially removed from the viral envelope, and no detergent molecules replace

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them. Applicant argues that the detergent removal methods that Barrett discloses are suitable for reducing concentration of detergent molecules in the solvent phase, however, the molecules entrenched in by their hydrophobic interactions with proteins in the envelope of the inactivated particles in Barrett are not necessarily removed by these methods.

- In response to Applicant's arguments, the Office notes that Barrett states the following at column 5, lines 12-30:

According to a particular aspect of the present invention, the non-ionic detergent from the group of the polysorbates remains in the virus-containing solution after the inactivation step. Particularly for Tween® 80 it has been known that it is considered to be human compatible and frequently is used in food stuffs and cosmetics. Thus, in a vaccine to be administered to man or animal and comprising a more or less small amount of detergent, no side effects are to be expected. Since according to the present method a concentration of up to 20% of non-ionic detergent can be used for the inactivation of viruses, it is, however, advantageous in some instances to reduce the concentration of detergent in the final product or, optionally, to completely remove it therefrom. This may be effected by known measures, such as, e.g., dialysis or chromatographic procedures. Particularly suitable chromatographic procedures are ion exchange chromatography or gel filtration. However, all the methods described in the prior art for removal of non-ionic detergents from a solution are suitable. [emphasis added]

- Barrett discloses that removal of some of the detergent may be desirable in some instances. By removing the detergent, or at least some of the detergent from the solution, the resulting viral particles are expected to be affected at least to some extent by the removal process because the viral particles are in the solution and are subjected to the same conditions as the surrounding solution. Applicant's particles as claimed, only require that the particle be partially delipidated, induce an immune response, and have an epitope exposed that is not typically exposed.

Barrett's viral particles meet these limitations. The claim limitations do not recite enough structural limitations such that Barrett's particles are clearly outside of the scope of the claims.

- Applicant argues that Barrett does not teach or suggest the removal of detergent from the envelope of inactivated viruses because removal of detergent would defeat the advantages of the detergent-inactivation procedure disclosed in Barrett. Applicant argues that the detergent is necessary to stabilize the solubilized proteins in the detergent-treated viruses (Barrett, col. 2, lines 46-49).
 - The Office acknowledges that the particles of Barrett contain some detergent molecules that assist in stabilization of the solubilized proteins of the particles. However, the question of a structural difference remains. Do the detergent molecules in Barrett's particles render the particles themselves structurally distinct from the instantly claimed particles? The Office maintains its position that the use of a detergent, a surfactant, or any of the originally disclosed solvents are useful for delipidating the viral particles as instantly claimed. Further, although detergents are no longer included in the method of production, Barrett's method of delipidation with a detergent was encompassed by the previously claimed invention in terms of the use of a detergent and the time that the particles were exposed to the detergent. In view of these considerations, the presence of the detergent molecules in Barrett's particles do not appear to render the particles patentably distinct from those of Barrett.

- According to the MPEP 2113, the use of 35 U.S.C. 102/103 rejections for product-by-process claims has been approved by the courts.

“[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith.” *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

- Applicant points out that Barrett teaches that “the structural integrity and...the biological activity of the surface and the envelope proteins are not affected” (Barrett, col. 4, lines 46-49). Applicant notes that the organic solvent used in the instant claims results in “exposing antigens and/or forcing a structural modification in the viral protein structures, which when introduced in to the body would provoke an effective immune response” (see the instant specification, page 23, lines 13-15).
 - In response to Applicant’s argument, Barrett discloses that the structural integrity of the whole virus and in particular of the enveloping proteins as well as their biological activity, such as immunogenicity and antigenicity, are largely retained (col. 3, lines 16-22) when non-ionic detergents are used within the range of 1% and 25% (col. 4, lines 7-11). Barrett discloses that such a result was surprising because non-ionic detergents such as Triton® X-100 has been used to disintegrate viral particles (col. 3, lines 16-25). Although Barrett does not teach that a structural modification has taken place in the viral particles treated with 1% to 25% of a non-ionic detergent, the Office asserts that this is a naturally occurring because, according to Applicant, treatment of viruses with detergents/surfactants

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in the range of 0.5% to 2%, for example, produces the instantly claimed viral particles that have been structurally modified.

- The Office also notes that Applicant points to the specification's disclosure at page 7, lines 18-20, which states the following:

Other solvents or detergents such as B-propiolactone, TWEEN-80, and dialkyl or trialkyl phosphates have been used, either alone or in combination. Many of these methods, especially those involving detergents, require tedious procedures to ensure removal of the detergent before reintroduction of the treated plasma sample into the animal or human.

Although the specification outlines the difficulties involved in using TWEEN-80, the specification does not exclude its use.

Conclusion

7. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campbell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 8-14-07
Primary Examiner, TC1600